

WE CLAIM:

1. A method for diagnosing or monitoring a disease or condition comprising the steps of:

- (a) obtaining a biological sample from a patient to be diagnosed or monitored;
- (b) determining the quantity of a target marker in said biological sample,

wherein said target marker is:

- (i) a truncated disease-associated protein lacking its two N-terminal amino acids, wherein said truncated disease-associated protein is not human serum albumin;

- (ii) a truncated disease-associated protein lacking its two C-terminal amino acids;

- (iii) a truncated disease-associated protein lacking its two N-terminal amino acids and its two C-terminal amino acids;

- (iv) a diketopiperazine (DKP) comprising the two N-terminal amino acids of a disease-associated protein; or

- (v) a DKP comprising the two C-terminal amino acids of a disease-associated protein; or

- (vi) two or more target markers selected from those listed in (i) through (v) above;

provided that when only a single DKP is used as the marker, it will not be His-Pro DKP; and

- (c) determining if the quantity(ies) of said target marker(s) in said biological sample is(are) indicative of the presence, absence or status of the disease or condition.

2. The method of Claim 1, wherein said marker is a truncated disease-associated protein.

3. The method of Claim 1, wherein said marker is X-Y-DKP, wherein X-Y-DKP is a diketopiperazine composed of amino acids X and Y, and X and Y are the two N-terminal or the two C-terminal amino acids of a disease-associated protein.

4. The method of Claim 3, wherein X and Y are the two C-terminal amino acids of a disease-associated protein.

5. The method of Claim 4, wherein X-Y-DKP is Arg-Arg-DKP, Gln-Asn-DKP, Lys-Arg-DKP, Glu-Phe-DKP, Ser-Met-DKP, Cys-Asn-DKP, Lys-Ala-DKP, Gln-Asn-DKP, Gly-Leu-DKP, Ala-Ala-DKP, Trp-Pro-DKP, Asn-Ser-DKP, Leu-Pro-DKP, Asp-Arg-DKP, His-Gly-DKP, Gln-Gly-DKP, Glu-Ser-DKP, Asn-Pro-DKP, Lys-Leu-DKP, Pro-Cys-DKP, Asn-Lys-DKP, Asp-Arg-DKP, Ala-Pro-DKP, Arg-His-DKP or combinations of the foregoing.

6. The method of Claim 3, wherein X and Y are the two N-terminal amino acids of a disease-associated protein.

7. The method of Claim 6, wherein X-Y-DKP is N-acetyl-Ala-Ser-DKP, N-acetyl-Ala-phosphorylated-Ser-DKP, Asp-Ala-DKP, Glu-Ile-DKP, Glu-Val-DKP, Phe-Pro-DKP, Ala-Glu-DKP, Phe-Val-DKP, Gly-Ile-DKP, Met-Ala-DKP, Met-Asp-DKP, Glu-Lys-DKP, Gln-Thr-DKP, Ala-Val-DKP, Gly-Leu-DKP, Ala-Pro-DKP, Glu-Ala-DKP, Pro-Glu-DKP, Lys-Ser-DKP, Ile-Val-DKP, Gln-Tyr-DKP, Lys-Glu-DKP, Glu-Asp-DKP, Ala-Pro-DKP, Ala-Asn-DKP, Ala-Leu-DKP, Ser-Leu-DKP, Val-Leu-DKP, Val-His-DKP, Gly-His-DKP, His-Pro-DKP, Ser-Pro-DKP or combinations of the foregoing.

8. The method of Claim 3, wherein X-Y-DKP is N-acetyl-Ala-Ser-DKP, N-acetyl-Ala-phosphorylated-Ser-DKP, Asp-Ala-DKP, Arg-Arg-DKP, Gln-Asn-DKP or combinations of the foregoing.

9. The method of Claim 3, wherein X-Y-DKP is Asp-Ala-DKP, Met-Ala-DKP, Gln-Asn-DKP, Gly-Leu-DKP or combinations of the foregoing.

10. The method of Claim 3, wherein X-Y-DKP is Gly-Leu-DKP, Ala-Pro-DKP, Glu-Ala-DKP, Leu-Pro-DKP, Asp-Arg-DKP, His-Gly-DKP or combinations of the foregoing.

11. The method of Claim 3, wherein X-Y-DKP is Arg-His-DKP, His-Pro-DKP, Ser-Pro-DKP, or combinations of the foregoing.

12. The method of Claim 3, wherein X-Y-DKP is Gly-Leu-DKP, Pro-Glu-DKP, Gln-Gly-DKP, Glu-Ser-DKP, or combinations of the foregoing.

13. The method of any one of Claims 1-3, wherein said disease-associated protein is myelin basic protein, beta-amyloid, Rh factor, pulmonary surfactant-associated protein A, B or D, insulin, tau protein, alpha-synuclein, albumin, C-reactive protein, interleukin 8, S100 proteins,

beta-chorionic gonadotropin, fetal erythropoietin, pregnancy-associated protein A, myoglobin, troponin I, troponin T, prostate specific antigen, amylase, lipase, alpha1-antitrypsin, erythropoietin, activated protein C, tethal chain, zeta chain, alpha chain, beta chain, delta chain, epsilon chain, gamma AG and brain natriuretic peptide.

14. The method of any one of Claims 1-3, wherein the disease or condition is multiple sclerosis, rheumatoid arthritis, acute respiratory distress syndrome, cystic fibrosis, diabetes mellitus, Alzheimer's disease, Parkinson's disease, inflammation, ischemia, cerebral ischemia, placental ischemia, myocardial infarction, prostate cancer, pancreatitis, emphysema, renal disease, cancer, chemotherapy, hemoglobinopathies, anemias or congestive heart failure.

15. The method of Claim 1, wherein two or more target markers are quantitated.

16. A method of diagnosing or monitoring multiple sclerosis (MS) in a patient, comprising the steps of:

- (a) obtaining a biological sample from said patient;
- (b) measuring the amount of a MS diagnostic compound in said biological sample to diagnose or monitor said MS in said patient.

17. The method of Claim 16, wherein said MS diagnostic compound is:

- (i) a compound having a mass of about 175 as determined by liquid chromatography and mass spectrometry;
- (ii) a compound having a mass of about 145 as determined by liquid chromatography and mass spectrometry;
- (iii) Asp-Ala diketopiperazine (DA-DKP);
- (iv) N-acetyl-alanine-serine diketopiperazine (NAS-DKP); or
- (v) combinations of the foregoing;

wherein:

the absence of compounds (i) and/or (ii) or an elevated amount of DA-DKP and/or NAS-DKP in said biological sample is indicative of MS; and

an elevated amount of DA-DKP and/or NAS-DKP in said biological sample is indicative of active MS.

18. The method of Claim 17, wherein said MS is active MS.
19. The method of Claim 18, wherein said MS diagnostic compound is DA-DKP, NAS-DKP or both.
20. A method of diagnosing or monitoring Alzheimer's disease in a patient, comprising the steps of:
 - (a) obtaining a biological sample from said patient; and
 - (b) measuring the amount of an Alzheimer's diagnostic compound in said biological sample to diagnose or monitor said Alzheimer's disease.
21. The method of Claim 20, wherein said Alzheimer's diagnostic compound is:
 - (i) a compound having a mass of about 175 as determined by liquid chromatography and mass spectrometry;
 - (ii) Asp-Ala-DKP; or
 - (iii) both (i) and (ii).
22. A method of diagnosing or monitoring placental ischemia in a pregnant patient, comprising the steps of:
 - (a) obtaining a biological sample from said patient; and
 - (b) measuring the amount of a placental ischemia diagnostic compound in said biological sample to diagnose or monitor said placental ischemia.
23. The method of Claim 22, wherein said placental ischemia diagnostic compound is:
 - (i) Gly-Leu-DKP;
 - (ii) Ala-Pro-DKP; or
 - (iii) both Gly-Leu-DKP and Ala-Pro-DKP.
24. The method of Claim 1, 16, 20 or 22, wherein step (b) is conducted by mass spectrometry, chemical assay or immunoassay.
25. The method of claim 24, wherein step (b) is conducted by immunoassay.

26. The method of Claim 25, wherein said immunoassay is conducted by using one or more binding partners specific for a target marker, MS diagnostic compound, Alzheimer's diagnostic compound or placental ischemia diagnostic compound.

27. The method of Claim 26, wherein the binding partner is an antibody or an aptamer.

28. The method of Claims 1, 16, 20 or 22, wherein said biological sample is a body fluid.

29. The method of Claim 28, wherein said body fluid is serum, plasma, blood, urine, saliva, cerebrospinal fluid, tears, semen, vaginal secretion, amniotic fluid or cord blood.

30. The method of Claim 29, wherein said body fluid is plasma or serum.

31. The method of Claims 1, 16, 20 or 22, wherein said patient is an animal.

32. The method of Claims 31, wherein said patient is a human.

33. An isolated binding partner having specificity for a target marker selected from the group consisting of:

(a) a truncated disease-associated protein lacking its two N-terminal amino acids, wherein said truncated disease-associated protein is not human serum albumin;

(b) a truncated disease-associated protein lacking its two C-terminal amino acids;

(c) a truncated disease-associated protein lacking its two N-terminal amino acids and its two C-terminal amino acids;

(d) a diketopiperazine (DKP) comprising the two N-terminal amino acids of a disease-associated protein, wherein the DKP is not His-Pro DKP; and

(e) a DKP comprising the two C-terminal amino acids of a disease-associated protein, wherein the DKP is not His-Pro DKP.

34. The isolated binding partner of Claim 33, wherein the binding partner has specificity for a DKP.

35. The isolated binding partner of Claim 34, wherein the binding partner has specificity for Arg-Arg-DKP, Gln-Asn-DKP, Lys-Arg-DKP, Glu-Phe-DKP, Ser-Met-DKP, Cys-Asn-DKP, Lys-Ala-DKP, Gln-Asn-DKP, Gly-Leu-DKP, Ala-Ala-DKP, Trp-Pro-DKP, Asn-Ser-

DKP, Leu-Pro-DKP, Asp-Arg-DKP, His-Gly-DKP, Gln-Gly-DKP, Glu-Ser-DKP, Asn-Pro-DKP, Lys-Leu-DKP, Pro-Cys-DKP, Asn-Lys-DKP, Asp-Arg-DKP, Ala-Pro-DKP or Arg-His-DKP.

36. The isolated binding partner of Claim 34, wherein the binding partner has specificity for N-acetyl-Ala-Ser-DKP, N-acetyl-Ala-phosphorylated-Ser-DKP, Asp-Ala-DKP, Glu-Ile-DKP, Glu-Val-DKP, Phe-Pro-DKP, Ala-Glu-DKP, Phe-Val-DKP, Gly-Ile-DKP, Met-Ala-DKP, Met-Asp-DKP, Glu-Lys-DKP, Gln-Thr-DKP, Ala-Val-DKP, Gly-Leu-DKP, Ala-Pro-DKP, Glu-Ala-DKP, Pro-Glu-DKP, Lys-Ser-DKP, Ile-Val-DKP, Gln-Tyr-DKP, Lys-Glu-DKP, Glu-Asp-DKP, Ala-Pro-DKP, Ala-Asn-DKP, Ala-Leu-DKP, Ser-Leu-DKP, Val-Leu-DKP, Val-His-DKP, Gly-His-DKP, His-Pro-DKP or Ser-Pro-DKP.

37. The isolated binding partner of any one of Claims 33-36, wherein said binding partner is an antibody.

38. The isolated binding partner of Claim 35, wherein said antibody is a monoclonal antibody.

39. The isolated binding partner of any one of Claims 33-36, wherein said binding partner is an aptamer.

40. A composition comprising the binding partner of any one of Claims 33-39 in a physiologically-acceptable carrier.

41. A kit comprising the binding partner of Claim 33 and associated reagents for quantitating the target marker.

42. A kit comprising the binding partner of any one of Claims 34-36 and associated reagents for quantitating the DKP.

43. The kit of Claim 41 or 42, wherein said binding partner is an antibody.

44. The kit of Claim 43, wherein said antibody is a monoclonal antibody.

45. The kit of Claim 41 or 42, wherein said binding partner is an aptamer.

46. The kit of Claim 41 or 42, wherein said binding partner is specific for a MS diagnostic compound, an Alzheimer's diagnostic compound or a placental ischemia diagnostic compound.